

CLAIMS

What is claimed is:

1. An isolated polynucleotide molecule comprising a nucleotide sequence encoding an MLK4 gene product from a human, wherein the MLK4 gene product comprises the amino acid sequence of SEQ ID NO:2.
2. The isolated polynucleotide sequence of claim 1 comprising the nucleotide sequence of SEQ ID NO:1.
3. An isolated polynucleotide molecule that is homologous to a polynucleotide molecule comprising the nucleotide sequence of SEQ ID NO:1.
4. An isolated polynucleotide molecule consisting of a nucleotide sequence that is a substantial portion of a polynucleotide molecule comprising a nucleotide sequence encoding an MLK4 gene product from a human, wherein the MLK4 gene product comprises the amino acid sequence of SEQ ID NO:2.
5. The isolated polynucleotide molecule of claim 4, wherein the nucleotide sequence encoding the MLK4 gene product comprises the nucleotide sequence of SEQ ID NO:1.
6. An isolated polynucleotide molecule comprising a nucleotide sequence encoding a PAK4 gene product from a human, wherein the PAK4 gene product comprises the amino acid sequence of SEQ ID NO:4.
7. The isolated polynucleotide sequence of claim 6 comprising the nucleotide sequence of SEQ ID NO:3.
8. An isolated polynucleotide molecule that is homologous to a polynucleotide molecule comprising the nucleotide sequence of SEQ ID NO:3.
9. An isolated polynucleotide molecule consisting of a nucleotide sequence that is a substantial portion of a polynucleotide molecule comprising a nucleotide sequence encoding a PAK4 gene product from a human, wherein the PAK4 gene product comprises the amino acid sequence of SEQ ID NO:4.
10. The isolated polynucleotide molecule of claim 9, wherein the nucleotide sequence encoding the PAK4 gene product comprises the nucleotide sequence of SEQ ID NO:3.
11. An isolated polynucleotide molecule comprising a nucleotide sequence encoding a PAK5 gene product from a human, wherein the PAK5 gene product comprises the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:10.
12. The isolated polynucleotide sequence of claim 11, comprising the nucleotide sequence of SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9 from nt 199 to nt 2244, or SEQ ID NO:11 from nt 6125 to nt 17433.
13. An isolated polynucleotide molecule comprising the nucleotide sequence of

an exon of SEQ ID NO:7.

14. An isolated polynucleotide molecule that is homologous to a polynucleotide molecule comprising the nucleotide sequence of SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9 from nt 199 to nt 2244, or SEQ ID NO:11 from nt 6125 to nt 17433.

5 15. An isolated polynucleotide molecule consisting of a nucleotide sequence that is a substantial portion of a polynucleotide molecule comprising a nucleotide sequence encoding a PAK5 gene product from a human, wherein the PAK5 gene product comprises the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:10.

10 16. The isolated polynucleotide molecule of claim 15, wherein the nucleotide sequence encoding the PAK5 gene product comprises the nucleotide sequence of SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9 from nt 199 to nt 2244, or SEQ ID NO:11 from nt 6125 to nt 17433.

15 17. An isolated polynucleotide molecule comprising a nucleotide sequence encoding a YSK2 gene product from a human, wherein the YSK2 gene product comprises the amino acid sequence of SEQ ID NO:13.

18. The isolated polynucleotide sequence of claim 17, comprising the nucleotide sequence of SEQ ID NO:12.

19. An isolated polynucleotide molecule that is homologous to a polynucleotide molecule comprising the nucleotide sequence of SEQ ID NO:12.

20 20. An isolated polynucleotide molecule consisting of a nucleotide sequence that is a substantial portion of a polynucleotide molecule comprising a nucleotide sequence encoding a YSK2 gene product from a human, wherein the YSK2 gene product comprises the amino acid sequence of SEQ ID NO:13.

25 21. The isolated polynucleotide molecule of claim 20, wherein the nucleotide sequence encoding the YSK2 gene product comprises the nucleotide sequence of SEQ ID NO:12.

22. A recombinant vector comprising any of the polynucleotide molecules of claims 1, 6, 11 or 17.

23. A transformed host cell comprising the recombinant vector of claim 22.

30 24. A substantially purified or isolated polypeptide comprising a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:13.

35 25. A method of preparing a substantially purified or isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:13, comprising culturing host cells of claim 23 under conditions conducive to the expression of the polypeptide or peptide fragment, and recovering in substantially purified or isolated form the

polypeptide or peptide fragment from the cell culture.

26. An isolated antibody specific for a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:13.

27. The isolated antibody of claim 26 which is specific for amino acid residues 1-10 of SEQ ID NO:13.

28. A method of screening for compounds that affect the cellular levels of a JNKKK gene product, comprising:

- a) applying a test compound to a cellular test sample;
- b) determining the cellular level of at least one JNKKK gene product in the test sample wherein the gene product is a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:13 or an mRNA encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10 and SEQ ID NO:13; and
- c) comparing the levels of the gene product in the test sample with that in a reference sample;

wherein a specific change in the cellular levels of the gene product in the test sample as compared to the reference sample indicates that the compound affects the cellular levels of gene product from a JNKKK gene.

29. The method of claim 28, wherein the gene product is an mRNA.

30. The method of claim 28 further comprising the step of applying a stress event to the test sample, and determining the effect of the test compound on the response of the test sample to the stress event.

31. The method of claim 28, wherein the stress event is exposure to ultraviolet radiation.

32. The method of claim 29, wherein the stress event is exposure to an inflammatory cytokine.

33. The method of claim 28, wherein the test and reference samples are cultured cells.

34. The method of claim 28, wherein the test and reference samples are cultured skin tissues.

35. The method of claim 28, wherein the test and reference samples are animals.

36. A method of screening for compounds that affect the activity of a JNKKK, the method comprising:

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- a) applying a test compound to a test sample;
  - b) determining the activity of a JNKKK in the test sample and a reference sample, wherein the JNKKK comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:13;

10 wherein a test compound that alters the JNKKK activity in the test sample as compared to the reference sample is identified as a compound that affects the activity of the JNKKK.

37. The method of claim 36, wherein the step of determining the activity of the JNKKK comprises determining kinase activity of the JNKKK:

15 38. The method of claim 36, further comprising the step of applying a stress event to the test sample and determining the effect of the test compound on the response of the test sample to the stress event.

39. The method of claim 38, wherein the stress event is ultra-violet radiation.

40. The method of claim 38, wherein the stress event is an inflammatory cytokine.

20 41. The method of claim 36, wherein the test and reference samples are cultured cells.

42. The method of claim 36 wherein the test and reference samples are cultured skin tissues.

25 43. A method for identifying a compound that binds to a PAK5 polypeptide comprising the amino acid sequence of SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:10, or that binds to a YSK2 polypeptide comprising the amino acid sequence of SEQ ID NO:13, comprising:

- a) contacting a test compound with the polypeptide for a time sufficient to form polypeptide/compound complex; and
  - b) detecting the complex;
- 30 so that if a polypeptide/test compound complex is detected, a compound that binds to the PAK5 polypeptide or YSK2 polypeptide is identified.

44. A method of screening for compounds that affect the expression of a gene that encodes a JNKKK gene product, comprising:

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- (a) applying a test compound to a test sample;
  - (b) determining the expression level of at least one gene in cells of the test sample, wherein the gene encodes a JNKKK gene product comprising an amino acid sequence selected from the group

consisting of SEQ ID NOS:2, 4, 6, 8, 10 and 13; and

- (c) comparing the expression level of the gene in the test sample with that in a reference sample;

wherein a specific change in the expression of the gene in the test sample as compared to the reference sample indicates that the test compound affects the expression of the gene.

45. The method of claim 44, further comprising the step of applying a stress event to the test sample and determining the effect of the test compound on the gene expression response of the test sample to the stress event.

46. A method of detecting an MLK4-, PAK4-, PAK5- or YSK2-related polynucleotide in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the particular polynucleotide for a period of time sufficient to form the complex, and detecting the complex, so that if a complex is detected, the MLK4, PAK4, PAK5 or YSK2-related polynucleotide, respectively, is detected.

47. The method of claim 46, wherein the method comprises contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the particular polynucleotide under such hybridization conditions, and amplifying the annealed polynucleotides, so that if a particular polynucleotide is amplified, the MLK4-, PAK4-, PAK5- or YSK2-related polynucleotide, respectively, is detected.